Remarks

Claims 5, 13, 22 and 24 are under examination and non-final rejection. Claims 5 and 22 are amended herewith. Claims 14 and 23 are canceled. New claims 25 – 31 have been added. Support for the new claims can be found in Claim 5 as originally filed, as well as in multiple placed in the specification as filed. Thus, it is submitted no new matter has been added.

Applicants appreciate the Examiner's withdrawal of the previously imposed rejections under 35 USC 112.

Claim objections

It is believed the amendment to claim 5 obviates the objections based on parenthesis and use of the term CREST. While "CREST" now appears in new claim 28, Applicants respectfully submit that "CREST syndrome" has an ordinary meaning in the art and as such it is either not an acronym, or it should be excepted from the requirement for elaboration of an acronym. Specifically, it is well known in the art that the limited form of scleroderma is referred to as CREST syndrome, and that the term "CREST" refers to five main features of the disorder, namely Calcinosis, Raynaud's syndrome, Esophageal dysmotility, Sclerodactyly and Telangiectasia. The Examiner is respectfully requested to withdraw the objection.

Objection to the Abstract

Applicants have herewith amended the Abstract. Thus, the objection is rendered moot.

Indefiniteness

It is believed the amendments to claims 5 and 22 overcomes the rejections under 35 U.S.C. 112, second paragraph, based on the allegation of indefiniteness. The Examiner is requested to remove the rejection. .

As for the remaining claim rejections, Applicants respectfully disagree and request reconsideration for at least the following reasons.

Rejections - 35 USC 102(b)

Claims 5, 13, 22 and 24 stand rejected over Ansorge (WO 02/053170) based on the contention that this reference anticipates the instant claims.

In response, Applicants reiterate from the last response that the present claims are distinct from the reference of Ansorge because the claims specify that the inhibitors are administered to an individual in need of the recited therapy, and there is no such individual described in Ansorge.

Specifically, it is asserted in the Office Action:

> "The reference [Ansorge] teaches that the combination therapy utilizing dermatological illnesses by inhibition of DNA synthesis, meeting the limitation of claims 5, 13, 22 and 24."

Applicants respectfully point out that the quoted phrase is not a coherent sentence, and moreover, even assuming *arguendo* that the reference does teach "inhibition of DNA synthesis" it still does not teach the remaining limitations of the presently pending claims, either expressly or inherently. In particular, Ansorge does not anywhere disclose administering the recited combination to an individual who is in need of therapy for hyperproliferation of fibroblasts, which is required, for example, by present claim 13, and where the limitation is not present in a "wherein" clause. In this regard, Applicants submit that that the "wherein" clauses in the present claims do in fact limit the claims to particular structural features. The wherein clauses specify effects of practicing the method, and moreover, specify the patient population on which the method is practiced. Thus, all of the wherein clauses in the pending claims should be accorded patenatable weight. Accordingly, Ansorge does not disclose expressly or inherently administering the recited compositions to an individual in need of treatment for any of the conditions now recited in amended claim 5, previously presented claim 13, its dependents, or the newly added claims 25-31.

Applicants further point out it is conceded in the Office Action that Table 1 of Ansorge is not identical with the diseases treated by instant application. Applicants agree, and emphasize that the rejection relies on the contention that the administration described in Ansorge "**would treat other benign fibrotic and sclerotic diseases**." (Applicant's bolding.) Applicants submit that whether the methods disclosed in Ansorge "would treat" other diseases is immaterial to the

salient question of whether the reference of Ansorge does in fact expressly or inherently disclose such a treatment. Applicants respectfully submit it does not. The additional citation of the Castagnoli et al., Andriessen et al. and Machesney et al. references does not remedy the lack of express or inherent anticipation by Ansorge.

In more detail, it is asserted in the Office Action that the reference of Castagnoli et al teaches that sections from hypertrophic scars show an anomalous expression of HLA-DR molecules on keratinocytes and fibroblasts. From this, the Examiner contends that "both keratinoctyes and fibroblasts are involved in hypertrophic scars" and that this allegedly supports the conclusion that the reference of Ansorge somehow results in that which is presently claimed. However, there is no evidence in Castagnoli et al. or elsewhere on the record that expression of HLA-DR molecules on fibroblasts signifies that the fibroblasts are hyperproliferating in association with a dermatological disease. In fact, Castagnoli et al. states:

> "… the anomalous presence of class II molecules on fibroblasts may be related to the active role of these cells in the development of scar tissue, since they actively synthesize collagen … during the repair process of skin injury. At present, it is not known whether the DR molecules on non-immunocompetent cells (keratinocytes and/ or fibroblasts) convert the same cells into effective antigen-presenting cells in dermatological affections … ". (See page 353, left column, last paragraph).

Thus, the disclosure of Castagnoli et al. does not support the allegation in the Office Action that the reference of Ansorge inherently describes treatment of individuals in need of therapy for hyperproliferation of fibroblasts, or any of the conditions recited in previously pending claim 5, presently amended claim 5, or any of the new claims. The same rationale applies to Andriessen et al. and Machesney et al. – neither of these references provide evidence that the disclosure of Ansorge inherently results in what is claimed in the present case. Specifically, Andriessen et al. discloses that "… the pathogenesis of hypertrophic scarring includes excessive production of extracellular matrix (ECM) by wound healing fibroblasts, possibly under the influence of … high levels of fibrogenic cytokines, such TGF-ß" (page 192, right column, second paragraph). However, this is not a description of hyperproliferation of fibroblasts, and there is nothing on the record to show otherwise, including in the reference of Machesney et al.

Notwithstanding the foregoing, Applicants reiterate that the instant rejection is based on the contention that Ansorge "would treat" other diseases. This is not relevant to whether the reference of Ansorge actually does describe a method that inherently anticipates the present claims, which recite individuals who are in need of therapy for disorders that are conceded in the office action to be not the same as those described in Table 1 of Ansorge. As such, the rejection based on inherency over Ansorge cannot be maintained. In connection with this, the Examiner's attention is respectfully directed to MPEP § 2112, which sets forth the legal and technical requirements to properly present a rejection based on inherency. Specifically, it is stated in this section of the MPEP:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

Further, the same section of the MPEP also provides the following guidance that the Patent Office must abide by in order to show inherency:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." Quoting *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); emphasis in original.

Further still, MPEP § 2112 states:

> To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. **Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient**. (Applicant's emphasis.)

Thus, in view of the foregoing amendments to the claims, Applicants' remarks presented herewith, and the guidance provided by the MPEP on the requirements for a showing of inherency, Applicants respectfully submit that the Patent Office's burden in presenting a *prima facie* case of anticipation by inherency has not been met, and cannot be met since the present

invention is distinct from the disclosure of Ansorge. As such, the rejections over Ansorge should be withdrawn and the claims passed to allowance.

Applicants request a three-month extension of time to file this response. Any fees due may be charged (or any overpayment credited) to Deposit Account no. 08-2442.

Respectfully submitted,

/John D. Lopinski/

By: _____

John D. Lopinski, Reg. No. 50,846

HODGSON RUSS LLP
The Guaranty Building
140 Pearl Street, Suite 100
Buffalo, NY 14202-4040
Tel. 716-848-1628
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